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EXAMINER	
MOSHER, MARY	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No. 09/913,927	Applicant(s) SCHUBERT ET AL.	
	Examiner Mary E. Mosher, Ph.D.	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *7/1/2002, 9/9/2002, 11/20/2002, 3/4/2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *31-47* is/are pending in the application.

4a) Of the above claim(s) *40-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *21-39 and 44-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

Newly submitted claims 40-43 are directed to an invention that is independent or distinct from the invention originally claimed, because they do not relate to a single general inventive concept under PCT Rule 13.1. Under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The only technical feature common between claims 40-43 and 31-39, 44-47 is that both groups involve HIV VPR protein. This feature is not a special technical feature, because this feature is not novel (see for example the publication by de Roquigny cited in the previous Office Action). The peptides of claim 31 do not require the synthesis method of claim 40. The synthesis method of claim 40, and the product-by-process peptide of claim 43, do not require the specific sequences of claim 31. Also, the process of claim 40 produces a combination of two peptides, each attached to a resin, which is still another different technical feature lacking commonality with claim 31. The synthetic method requires search not required for examination of the peptides originally presented. Since there is no special technical feature which unites the two groups of claims, restriction is proper.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 40-43 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

Claims 33, 34, 36, 38, 44-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 recites "A synthetic peptide comprising....(SEQ ID NO:1), or a fragment or variant thereof, wherein the fragment or variant thereof consists of ...". It is not clear if

"comprising" refers only to SEQ ID NO:1, or if it also refers to the recited fragments and variants. In one interpretation, the claim is open to peptides (of any length) comprising any 15 amino acids of (a)-(c); in the other interpretation, the claim is limited to peptides (a)-(c), fragments of (a)-(c) with no unrelated sequence, and peptides comprising SEQ ID NO:1. Which scope is intended? This affects dependent claims 33, 34, 36, 38, 44, and 46.

In addition, in claim 31, parts (b) and (c), it is not clear if the peptide is a fragment of SEQ ID NO:1, or a variant which includes residues 1-47 or 48-96 of any VPR sequence. This also affects the scope of the claim, and affects dependent claims 36, 38, and 44-47.

Also, claims 44-47 are drawn to a "system", which is not one of the statutory categories of patentable subject matter. Are the claims directed to a composition of matter or to an assay method?

Claims 34, 35, 38, 39, and 44-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. For claims 34, 35, 38, and 39, applicant points to page 12, lines 12-22, and pages 2-5, but these passages do not reasonably convey the broad concept of "bound to a second molecule comprising a DNA or protein molecule." For claims 44-47, applicant point to page 11, lines 13-22; however, the general discussion of "serological test systems, specifically VPR antigen (Ag) ELISA, as standard antigen for calibration of VPR - Ag ELISA -techniques..." does not reasonably convey the concept of immobilized antigen, as claimed; in fact, the discussion of "detection and quantitation of viral VPR in blood samples" conveys, if anything, the concept of immobilized antibody, not immobilized VPR antigen. The remaining discussion of various possible tests systems do not reasonably convey the concept of the peptide immobilized on a substrate. Therefore, "bound to a

second molecule comprising a DNA or protein molecule" and an assay with the peptide "immobilized on a substrate" are seen as new matter.

Claims 36-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims are drawn to a pharmaceutical composition. The specification does not teach any treatment method using the claimed peptides, and search of the prior art does not indicate routine knowledge of successful treatment methods using HIV VPR peptides. Considering the absence of guidance, the undeveloped state of the art, and the quantity of experimentation required to develop a therapeutic method using the claimed pharmaceutical composition, it is concluded that undue experimentation would be required to use the pharmaceutical compositions as claimed.

Claims 31, 34, 36, 38, 44, 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the recited VPR fragments, does not reasonably provide enablement for variant peptides SEQ ID NO:8 and 9.. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification asserts various uses for VPR peptides, see for example page 10 line 21 through page 12 line 23. However, the specification does not suggest how to use variant peptides which do not match the sequence of VPR from any known strain of HIV. Therefore, after reading the specification, it is not apparent how to use the peptides of SEQ ID NO:8-9, other than for further research. Considering the limited teachings of the specification, the absence of any information about the biological properties of the variant peptides, and the absence of any working example indicating how to use the variant peptides, it is concluded that undue experimentation would be required to use the full scope of the invention as claimed.

Claim Rejections - 35 USC § 102

Claims 31, 32, and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Azad et al WO 95/26361. Azad teaches peptides 2, 3, and 5 on page 15, which consist of a fragment of residues 48-96 of SEQ ID NO:1. See also page 23, lines 24-31, which teaches a composition comprising peptide 3 in PBS; PBS is a well-known pharmaceutically acceptable carrier. Azad also teaches synthesis of the full-size VPR of strain NL4-3 in yeast cells, see pages 10-12, and teaches a VPR sequence identical to SEQ ID NO:1, see figure 6.

Claim 31 is rejected under 35 U.S.C. 102(b) as being anticipated by Sette et al WO 98/32456. See Table VII, page 38, which teaches two peptides that are fragments of VPR 48-96.

Claims 31, 34, and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Koprowski et al WO 98/08375. Hooper teaches a synthetic peptide comprising SEQ ID NO:1 bound to a plant virus coat protein and immobilized on a nylon membrane. See pages 4, 28-30.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 35 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Azad et al WO 95/26361. As discussed above, Azad teaches synthesis of the NL4-3 VPR protein in yeast cells, and there is reason to believe that the NL4-3 VPR protein is identical to SEQ ID NO:1. These claims differ from the above in requiring binding to a second molecule or in requiring a pharmaceutically acceptable carrier. Azad explicitly suggests linkage of the VPR protein to a carrier, see page 6, lines 21-24. Azad also explicitly suggests treating diseases caused by pathogens by administering VPR protein to a mammal, see page 5, line 18-22. Since treatment processes routinely use pharmaceutically acceptable carriers, the composition comprising the protein and a pharmaceutically acceptable carrier is seen as obvious. Considering the explicit

suggestions made by Azad, the invention as a whole is seen as prima facie obvious, absent unexpected results.

Claims 33, 34, 37, 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sette et al WO 98/32456. Sette teaches peptides containing epitopes which bind MHC class II molecules of multiple HLA types, and use of the peptides to induce a helper T lymphocyte response. The peptides are useful because they are not limited to persons of one HLA type. Sette also suggests immunogenic peptide conjugate compositions containing the peptides as helpers in combination with peptides which induce a cytotoxic lymphocyte response, see for example page 5. Sette teaches two HIV VPR peptides that consist of residues 57-71 and 58-72 of VPR, see Table VIII on page 38. This differs from SEQ ID NO:7 only in that the reference peptides are shifted one or two residues within the VPR sequence. However, one of ordinary skill in the art would reasonably expect that a substantially overlapping peptide, like SEQ ID NO:7, would have similar useful properties, and could be used in similar ways. The claimed peptide is therefore seen as an obvious variant, absent unexpected results.

Claims 31-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weiner et al WO 96/08970. Wiener teaches that VPR translocates into the nucleus of cells when it bings to rip-1, see for example page 36. Wiener suggests conjugation of molecules such as DNA to VPR or rip-1-binding fragments of VPR, see for example pages 36-38, and suggests use of the conjugates for treatments in vivo. Wiener suggests use of VPR from NL-43, see page 13 lines 3-5. Weiner also teaches a rip1-binding VPR fragment 41-55, see page 53 lines 15-17. Although Weiner does not teach the detailed structure of VPR or fragments, it would have been obvious to use the sequence from NL-43 as suggested, resulting in a VPR sequence identical to applicants SEQ ID NO:1 and a peptide fragment identical to applicants SEQ ID NO:5. It further would have been obvious to use this peptide in the manner suggested. The invention as a whole is therefore prima facie obvious, absent unexpected results.

SEQ ID NO:8 and 9 are free of the art, as the prior art does not teach or suggest VPR peptides with these precise sequences.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone numbers for this Group are now (703) 872-9306 for Before Final responses, and (703) 872-9307 for After Final responses. Faxes for this Group can also be sent to (708) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

8/22/03

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800 1600